

PEER REVIEW HISTORY

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ARTICLE DETAILS

TITLE (PROVISIONAL)	Efficacy of hypnotherapy compared to cognitive behavioural therapy for mild to moderate depression – study protocol of a randomised controlled rater-blind trial (WIKI-D)
AUTHORS	Fuhr, Kristina; Schweizer, Cornelia; Meisner, Christoph; Batra, Anil

VERSION 1 - REVIEW

REVIEWER	Xinyu Zhou Department of Psychiatry, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China;
REVIEW RETURNED	14-May-2017

GENERAL COMMENTS	<p>The authors have written about an understudied and very important clinical topic: "Efficacy of hypnotherapy compared to cognitive behavioural therapy for mild to moderate depression – study protocol of a randomized controlled rater-blind trial (WIKI-D)". There are few data on this important topic and therefore this topic is interesting for future publication. However, in the current form presented, it requires a minor revision before consideration for publication.</p> <p>General comment The whole protocol should be in the future tense (except for the background where you are discussing previous findings).</p> <p>Introduction :</p> <ol style="list-style-type: none">1. The introduction need to introduce the epidemiological data, for providing the readers with a convincing argument as to why is it important for this study to be conducted.2. I would suggest changing the wording "success rates" to "response rate". <p>Methods and Analysis Exclusion criteria: 1. Why need to exclude diagnosis of chronic MDD (duration ≥ 2 years)? What is the standard definition of "chronic MDD"? Please add the reference. In addition, please clarify the reason why you exclude the patients with the diagnosis of chronic MDD.</p> <p>Assessments: 1. Please delete the duplicated words "Harvard" in the Harvard Group Scale of Hypnotic Susceptibility (page 11, last paragraph).</p> <p>Statistical Analysis: 1. The detailed data analytical plan should be added. How univariate analysis and multivariate analysis will be performed? Will confounding variables be controlled for? How?</p>
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REVIEWER	Associate Professor Sue Luty Department of Psychological Medicine, University of Otago, Christchurch, New Zealand
REVIEW RETURNED	15-May-2017

GENERAL COMMENTS	<p>This is a well thought out study and provides a comparison of 'gold standard CBT' with hypnotherapy</p> <p>The major revision reflects the issues of grammar and english language which repeat throughout the manuscript. I suggest a proof read for English and spelling and also you move between past and present tense. There is also some clumsy sentencing e.g. lines 42 - 48. A common error is to miss out the word 'the' and to use the word 'symptomatic' instead of symptoms.</p> <p>when introducing and describing hypnotherapy you need to explain further what you mean by 'representative technique' - line 58</p> <p>In line 13 p6 you mention personality related features then talk of sociodemographic variables. this does not make sense - the list you give is sociodemographic.</p> <p>IN the interventions it is not clear how many the therapists treated - probably because of the English. Did therapists treat both conditions - if so in treatment integrity you need to discuss this further.</p> <p>Who measured adherence to the manual in the recorded sessions and How was this done - what measure was used?</p> <p>In the description of the therapy your explanation of hypnotherapy is very confusing and not easily understood - what for example is adequate solution approaches? - line 19 p10.</p> <p>p 12 you do not explain why you measure the working alliance at week 6.</p> <p>The discussion appears reasonable</p>
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VERSION 1 – AUTHOR RESPONSE

Reviewer 1's Comments

General comment

#2. The reviewer suggested writing the whole protocol in the future tense.

Our response: We now have checked the whole manuscript and (except for the introduction) changed the tense into future tense:

- Abstract, Methods and Analysis, we changed 'we expected...' into 'we expect...'.
- Abstract, strengths and limitations: we replaced 'could' and 'were' in the last sentence with 'will': 'The therapists and patients will not be blinded...(…) whereas the raters of the follow-up assessments will be blind...'
- Introduction, Objectives: we replaced the verbs 'is' and 'are' with 'will be', see revised text marked in yellow
- Methods and Analysis: except for the paragraphs concerning the sample size and power calculation as well as the description of the interventions (because it was already conducted before) we changed the past or actual tense into future tense highlighting the changes in yellow.
- Discussion: we also changed the tense into future tense regarding the potential results and contribution of the study to the field.

Introduction

#3. The reviewer suggested introducing the epidemiological data in the introduction.

Our response: We appreciate this suggestion and now included a sentence concerning the years lived with disability on p. 4, lines 27ff: 'Regarding the years lived with disability (YLD) as assessed by the WHO, mental disorders are the first cause for chronic conditions in the population of Europe. In Europe, unipolar depressive disorder is the first and leading reason for chronic condition, leading alone 11% of all YLD [5].'

#4. The reviewer suggested changing the wording 'success rates' to 'response rates'.

Our response: We now did so in the Introduction, page 4, line 29 and in the Objective no. 5), page 6, line 49: 'Variables predicting treatment response will be analysed'.

Methods and Analysis

Exclusion criteria:

#5. The reviewer asked why we excluded patients with the diagnosis of chronic MDD and to clarify the reason for the exclusion. He also asked for the definition of "chronic MDD" together with a reference.

Our response: We decided to therefore include the following statement within the introduction on p. 4, lines 21 ff.: 'For chronic major depression with a duration of two years or longer, as well as for severe unipolar episodes, long-term psychotherapy is needed and yet the evidence concerning psychotherapy is ambiguous [3].'

Assessments

#6. The reviewer suggested deleting the duplicated words 'Harvard' in the title of the description of the HGSHS.

Our response: We now did so, see p. 13, line 25.

Statistical Analysis:

#7. The reviewer suggested adding the detailed data analytic plan. He asked whether and how univariate and multivariate analyses will be performed and if and how we will control for confounding variables.

Our response: We now added another paragraph concerning also the analysis of the secondary endpoints on page 17.

Reviewer 2's Comments

#8. The reviewer suggested a proof read for English and spelling and also stated that we moved between past and present tense. The reviewer stated that there is 'some clumsy sentencing, e.g. lines 42-48'. She recommended using for example the word 'the'. She also recommended using the word 'symptoms' instead of 'symptomatic'.

Our response: We now changed the word 'symptomatic' into 'symptoms' at the following places:

- Objectives, p. 6, line 13
- Sample size and power calculation, on p. 9, line 51
- The primary endpoint, on p. 12, line 8
- PHQ, on p. 12, line 25
- Study procedure, p.14, line 21, and on p. 14, line 55
- Methods for the assessment of safety, on p. 18, line 33

Relating also to the reviewer 1's general comment, we now checked the whole manuscript and changed the tense into future tense regarding the conduction of our study. We therefore carefully went through the whole manuscript and also commissioned a native English for proofreading. We have marked all the changes in yellow without hereby referring to all changes we have made in detail. We did however not find the related page concerning the 'clumsy sentencing' and were therefore unable to correct the sentence. However, we hope that with the proofreading of the English of the whole manuscript we have already covered that point.

#9. The reviewer stated that when describing hypnotherapy we need to explain what we mean by 'representative technique', p. 4, line 58.

Our response: With this technique we for example described using an animal or landscape or another 'agent' that best represents the current problem. We therefore give these examples in the text in parentheses to explain what we intended to say (in the marked copy manuscript: p. 5, line 25).

#10. The reviewer suggested mentioning 'sociodemographic variables' instead of 'personality related features' on p.6, line 13 (in the revised manuscript/ marked copy: p. 6, line 53).

Our response: We agree with the reviewer and now changed the phrase accordingly for the sociodemographic and the disorder-related variables (on p.7, line 7).

#11. The reviewer asked how many the therapists treated and if therapists treat both conditions.

Our response: We therefore changed the paragraph on p. 10 (interventions), lines 41ff: 'Overall, four therapists with adequate qualification (education in behavioural therapy or hypnotherapy and at least 3 years of professional experience) each in ACDT and HDT will be trained (1 – 2 days) related to the treatment manuals. Each therapist (four therapists per treatment condition) will treat 20 patients within the scope of the study.'

#12. The reviewer asked who measured adherence to the manual and how this was done.

Our response: We now added more information concerning the adherence process in the study on p. 10, lines 54ff: 'Therapists' adherence to the manual will be enhanced by regular supervisions on a monthly basis. Adherence to the manual will be tested by a therapist that is not involved in the study procedure. Thus, randomly chosen, digitally recorded sessions will be evaluated regarding treatment adherence based on a list of the relevant techniques of the given treatment manual.'

#13. The reviewer stated that the description of the hypnotherapy is very confusing.

Our response: We agree with the reviewer and now tried to give examples and clearer definition to this paragraph on p. 11, lines 35-44 (in the revised manuscript) as well as in the introduction (see also our response to her comment #3): 'The modules of the HDT promote hypnotic activation and reinforcement of own resources, the use of relevant positive and negative experiences from the biography, and the development of positive solution imagery. Furthermore, formal trance induction, utilisation techniques, indirect techniques such as the use of metaphors or the representative technique, or work with time progression will be used.'

#14. The reviewer suggested explaining why we measure working alliance at week 6.

Our response: We now included a sentence explaining the reason for this decision on p. 13, lines 40 ff: 'The assessment of the WAI early in therapy was chosen because this is a better predictor for therapy outcome [36, 37].'

We also included the new references [36, 37] in our reference list.

Once again, we appreciate your invitation to revise our manuscript for consideration for publication in BMJ Open. We are delighted that the two reviewers offered these positive comments about the importance of this study protocol. We found both all the comments extremely helpful in further strengthening our manuscript. We have considered each comment seriously, have made revisions to the manuscript as indicated, or otherwise have offered detailed explanation of reasons for not making changes in response to specific comments.

We look forward to your further consideration of this revised manuscript.

VERSION 2 – REVIEW

REVIEWER	Zhou Xinyu Department of Psychiatry, The First Affiliated Hospital of Chongqing Medical University, Chongqing, China
REVIEW RETURNED	02-Jul-2017

GENERAL COMMENTS	The authors clarify all my remarks and therefore I suggest to accept it. Regards!
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REVIEWER	Associate Aprofessor Sue Luty University of Otago Christchurch, New Zealand
REVIEW RETURNED	05-Jul-2017

GENERAL COMMENTS	This is a well designed trial and will add to the evaluation of a range of treatment options for depression
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